trimethylated (Fig. 1c). The combination of these two post-translational modifications is called H3K4me3Q5ser. Given that the modified lysine and glutamine residues are adjacent, the stability (or half-life) of the two modifications might be co-dependent. This proximity might also aid the recruitment of specialized chromatin-remodelling protein complexes. Indeed, the authors' findings suggest that H3K4me3Q5ser might help the function of the transcription factor TFIID, which acts on chromatin to promote transcription.

These findings raise other compelling questions. Does TGM2 have a role in the function of the enzymes that methylate H3K4, such as MLL1? If so, future studies should try to clarify the functional interplay between these enzymes. Does serotonylation of H3Q5 influence other post-translational modifications, in a similar way to how the trimethylation of H3K4 and the acetylation of lysine residues at positions 9 and 14 of histone H3 influence each other<sup>12</sup>? Are the intracellular pools of serotonin replenished in different ways depending on how serotonin is being used in various cellular compartments at any given time? Does extra-nuclear serotonin influence the serotonylation of histones by being transported into the nucleus on demand?

Serotonylation of histones and its potential influence on transcription might be only the tip of the iceberg in an ever-expanding scenario of post-translational modifications associated with chromatin changes. Histaminylation and dopaminylation (addition of histamine, an amino acid, and dopamine, a neurotransmitter, respectively) are likely to join the party, which could complicate the task of deciphering the language of histone modifications. However, an exciting road to discovery seems to lie ahead.

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# Improved charge carrying for solar cells

The commercialization of a promising class of solar cell has been hindered by issues associated with the components needed to construct it. A possible solution has now been reported. SEE LETTER P.511

# LIYUAN HAN

The most promising technology for the next generation of solar cells is based on a class of material known as perovskites. Perovskite solar cells can convert light into electricity with high efficiency (about 22%)<sup>1</sup>, but only when polymers known as polytriarylamine (PTAA) or 2,2',7,7'-tetrakis(N,N-di-p-methoxyphenylamine)-9,9'-spirobifluorene (spiro-OMeTAD) are used to transport holes – quasiparticles that bear a positive charge and are produced as part of the power-generating mechanism — within the cells. The high cost of these polymers limits their use in commercial solar cells. Another issue is that trace quantities of compounds called dopants need to be added to the polymers to enhance hole transport, but such dopants cause degradation of the perovskite layer in the devices<sup>2,3</sup>. On page 511, Jung et al.<sup>4</sup> report an architecture for a perovskite solar cell that uses a cheaper, dopant-free

polymer as the hole-transport material, and that has a truly impressive efficiency of 22.7%.

The problems associated with PTAA and spiro-OMeTAD have stimulated the search for alternatives. Cheaper, dopant-free materials for transporting holes have been reported<sup>5-7</sup>, as well as new stable dopants<sup>8</sup>, but the power-conversion efficiencies of perovskite solar cells made using these materials cannot compete with those of devices that use PTAA or spiro-OMeTAD. Finding low-cost hole-transport materials that provide both high efficiency and stability, and that are compatible with the industrial processes used to make solar cells, remains challenging.

One alternative candidate is poly(3-hexylthiophene) (P3HT; ref. 2). This polymer is cheap, has optoelectronic properties that are perfect for solar cells, and could be used in industrial-scale manufacturing processes. However, no efficiencies higher than 20% have been reported for perovskite solar cells made using P3HT. To understand the problems



**Figure 1 An extra layer for perovskite solar cells.** In solar cells, light absorbed by an active material, such as a perovskite, generates electron–hole pairs; holes are quasiparticles formed by the absence of an electron. The electrons and holes separate and pass through electron- or hole-transport materials, respectively, until they reach an electrode. In this example, the holes pass through to a gold electrode, whereas the electrons travel to a transparent conducting film that acts as an electrode. A current is generated when the electrodes are connected to a circuit. The polymer poly(3-hexylthiophene) (P3HT) is a cheap hole-transport material, but solar cells made using P3HT have had low power-conversion efficiency. Jung *et al.*<sup>4</sup> inserted a material called *n*-hexyl trimethyl ammonium bromide (HTAB) between P3HT and the perovskite layer. Interdigitation of molecular chains in HTAB and P3HT causes the polymer to self-assemble into fibrils that have excellent hole-transport properties, thereby increasing the efficiency of the solar cell. The extra layer also improves the stability of the device.

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**Figure 2** | **The bulk structure of a hole-transport material. a**, The polymer P3HT can be used to transport charge carriers called holes in solar cells, and is typically amorphous. **b**, Jung and colleagues' process<sup>4</sup> for making solar cells causes P3HT to self-assemble into fibrils. Hole mobility in fibrillar P3HT is about 10,000 times higher than in the amorphous form. Scale bars, 600 nanometres.

associated with P3HT, let's consider how hole-transport materials are used in perovskite solar cells.

The general principle of solar cells is that light absorbed by an 'active' material, such as a perovskite, generates a pair of charge carriers — a negatively charged electron and a positively charged hole (Fig. 1). These charge carriers are then separated and carried to different electrodes in a circuit, thereby generating a current. One way of achieving all this is to sandwich the perovskite between a material that carries the holes to an electrode and another material that carries the electrons to a separate electrode.

Part of the problem with using P3HT as the hole-transport material is that it makes only poor physical contact with perovskites, which limits the transfer of holes between the materials<sup>9</sup>. Another issue is that electrons and holes can recombine — a process called non-radiative recombination — at the perovskite–P3HT interface<sup>10</sup>, which results in energy losses.

Jung and colleagues' innovation is to overlay the perovskite layer with a material that conducts electrons poorly; the authors refer to this material as a wide-bandgap halide (WBH). The WBH blocks the transfer of electrons between the perovskite layer and P3HT, and therefore reduces charge recombination at the interface.

The WBH layer was formed *in situ* by the reaction of a compound called *n*-hexyl trimethyl ammonium bromide (HTAB) with the surface of the perovskite layer. The molecules that comprise HTAB consist of a hydrophilic head connected to a hydrophobic tail. The tails of HTAB interact strongly with the hydrophobic side chains of P3HT, as a result of van der Waals forces (Fig. 1). These interactions cause the molecules in P3HT to self-assemble into fibrils on the surface of the WBH (Fig. 2).

The bulk structure of P3HT affects its charge-transporting properties: hole mobility in fibrillar P3HT (ref. 11) is about 10,000 times higher than that in the amorphous form of the material<sup>12</sup>. This meant that Jung *et al.* did not need to use dopants in their solar cells to improve hole transport. Moreover, the HTAB

molecules effectively neutralize charged defects on the surface of the perovskite crystal. This neutralization helps to reduce the amount of charge recombination that occurs at the perovskite–P3HT interface.

The combined effects of using a fibrillar WBH layer in the perovskite solar cells enabled Jung and colleagues to obtain the outstanding efficiency of 22.7%. Their cells showed greatly improved stability compared with a control device that lacked a WBH layer — a WBH-containing cell encapsulated in plastic maintained more than 95% of its initial power-conversion efficiency after 1,370 hours of continuous illumination using light that simulates the intensity and spectrum of sunlight at Earth's surface. This stability can be attributed to the use of dopant-free P3HT. Non-encapsulated cells also showed greater moisture resistance than did unencapsulated control devices lacking WBH, as a result of the hydrophobic tails of HTAB.

Finally, Jung and co-workers showed that two widely used industrial methods for preparing thin films of material — spin coating and bar coating — could be used to prepare modules of perovskite coated with WBH and P3HT, with an area of about 25 square centimetres. By comparison, the solar cells characterized in the rest of the study had an area of about 0.09 cm<sup>2</sup>. Solar cells made from the larger modules using both industrial methods all had almost identical power-conversion efficiencies, indicating that the authors' solar-cell architecture could be reliably mass-produced for commercial applications.

The low cost and remarkable efficiency of perovskite solar cells make it reasonable to assume that such devices will become a commercially viable alternative to silicon solar cells, which are widely used at present. The greatest challenge to their commercialization is stability — more work is needed to improve the stability not only of perovskites, but also of the charge-transporting materials and the electrodes. By demonstrating how P3HT can be used as a stable and effective charge-transporting material, Jung and colleagues might have helped to accelerate the progress of perovskite solar cells to the market.

<sup>466 |</sup> NATURE | VOL 567 | 28 MARCH 2019 © 2019 Springer Nature Limited. All rights reserved.

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- Crosstalk between dengue and Zika

The factors that contributed to the explosive nature of the 2015 Zika outbreak in the Americas are not well understood. A new analysis explores the link between prior dengue virus exposure and Zika virus infection.

# STEPHEN S. WHITEHEAD & THEODORE C. PIERSON

ika virus (ZIKV) was discovered in Africa in 1947. Its impact on public health seemed restricted to sporadic local outbreaks associated with an illness characterized by mild fever<sup>1</sup>. But in 2013–14, ZIKV was introduced into the Americas, where it spread quickly. The large number of infections that occurred during the resulting epidemic revealed a previously unappreciated link between ZIKV infection of pregnant women and a devastating congenital neurodevelopmental disease in their babies<sup>2</sup>. The factors contributing to the rapid spread and disease severity observed in this outbreak remain elusive. Writing in Science, Rodriguez-Barraquer et al.<sup>3</sup> provide a highresolution view of the epidemiology of Zika disease in a Brazilian community during the 2015 epidemic. They also explore how prior infection with a related mosquito-borne virus contributes to the risk of ZIKV infection and disease.

ZIKV belongs to a group of evolutionarily related flaviviruses that includes yellow fever virus and dengue virus (DENV). Flavivirus infection triggers the production of antibodies (also called immunoglobulins), some of which can neutralize the virus's ability to infect cells. Antibodies can also coordinate other components of the host's immune response that destroys virus-infected cells, even when they cannot inhibit virus infection directly. Some antibodies are specific for a single flavivirus type, whereas others react against several flavivirus species (this is called cross-reactivity). The extensive antibody cross-reactivity against flaviviruses has complicated the development of laboratory diagnostics to identify individual virus types<sup>4</sup>.

Antibodies help to protect individuals against flavivirus infections. Nonetheless,

in rare circumstances, antibodies elicited by DENV infection might exacerbate dengue disease in people infected for a second time with a different variety (serotype) of DENV<sup>5</sup>. DENV circulates in many of the same parts of the world as ZIKV, including South and Central America. The unexpected appearance of congenital disease following the introduction of ZIKV into the Americas raised the possibility that cross-reactive antibodies produced during a prior exposure to DENV worsen the severity of Zika through similar mechanisms to those that increase the severity of dengue after a second DENV infection<sup>6</sup>.

Rodriguez-Barraquer *et al.* investigated the dynamics of a Zika outbreak in a DENVendemic region of Brazil. The study focused

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on a community of people living in the city of Salvador who were taking part in a long-term study of DENV. Because molecular assays provide a limited window in which to diagnose infection, the authors opted to use serological assays to measure antibody levels at different time points. They measured the levels of antibodies against ZIKV in individual serum samples collected before, during and after the 2015 Zika epidemic to establish the prevalence of infection among the study population.

Antibodies are grouped into five classes and several subclasses. The anti-ZIKV antibody response includes molecules that react against a protein called NS1, which is encoded by the virus but does not form part of the viral particle (virion). ZIKV NS1-reactive IgG3 antibodies are only transiently present in serum, partly because they have a short half-life *in vivo*<sup>7,8</sup>. Therefore, the presence of these antibodies in serum has been suggested to be a signal of a recent ZIKV infection<sup>7</sup>.

Rodriguez-Barraquer and colleagues observed that most of the serum samples collected before ZIKV was introduced into the studied population did not contain ZIKV NS1-reactive IgG3 antibodies. However, most samples contained these antibodies within five months of the first report of Zika in Salvador. The authors estimate that 73% of the community was infected with ZIKV by October 2015.



**Figure 1** | **Effect of dengue immunity on Zika virus infection.** Rodriguez-Barraquer *et al.*<sup>3</sup> measured the levels of antibodies (antibody titres) against Zika virus (ZIKV) and dengue virus (DENV) in individual serum samples from people in the Brazilian city of Salvador. They estimated the probability of ZIKV infection during the 2015 Zika outbreak on the basis of levels of total IgG antibodies against the DENV NS1 protein in samples collected in March 2015, before the outbreak (left-hand graph). The authors observed that the probability of ZIKV infection decreased with increased levels of anti-DENV IgG antibodies, which suggests that DENV exposure has a protective effect against future ZIKV infection. However, they also observed a correlation between increased levels of the IgG3 subset of antibodies against the DENV NS1 protein, which are thought to be a sign of recent DENV infection, and an increased risk of ZIKV infection (right-hand graph). Antibody titres are shown in a logarithmic scale, and pale red and blue areas denote 95% confidence intervals.